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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
SHARAREH, SHAHNAM J	
ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 08/29/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/933,316	PORTER, STEPHEN C	
	Examiner	Art Unit	
	Shahnam Sharareh	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *8/20/2001, 2/6/2003, 6/12/03* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-37* is/are pending in the application.

4a) Of the above claim(s) *6,12-14 and 29-37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,7-11 and 15-28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 2 .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other:

DETAILED ACTION

Election/Restrictions

1. Applicant's election of species of claims in Paper No. 7, wherein the non-cyanoacrylate rheology-modifying agent is the polymer is acknowledged. Accordingly, claims 1-5, 7-11, 15-28 read on the elected species and are under consideration. Claims 29-37 are withdrawn from further consideration for the reasons set forth in Paper Nos. 3, 6 and pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 5. Claims 6, 12-14 are also withdrawn from further consideration because they are directed to the nonelected species. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

2. Claims 1-5, 7-11, 15-28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

3. Claim 1 and all dependent claims thereof are rejected because it recites the broad recitation "a non-cyanoacrylate rheology modifying agent," and "a plasticizer" which is the narrower limitation for "a non-cyanoacrylate rheology modifying agent."

A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent protection desired. Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949).

4. The present claim 1 recites the broad limitation of "a non-cyanoacrylate rheology modifying agent." Yet, the claim also recites "a plasticizer" which is the narrower statement of non-cyanoacrylate rheology modifying agents. The non-cyanoacrylate rheology-modifying agent as described in page 6, lines 9-15, include such compounds that demonstrates plastic fluid behavior. In fact, instant claim 9 is directed to such compositions where the non-cyanoacrylate rheology modifying agent is the same as the plasticizer. Thus, claim 1 constructively comprises a broad and a narrow range of the same element. The limitation "non-cyanoacrylate rheology modifying agent" is a broader genus of the claimed plasticizers. Accordingly similar to the reasoning in *Ex parte Wu*,

the metes and bounds of the claims are not clear because a broad range or limitation together with a narrow range or limitation in the same claim is considered indefinite.

5. The term "high" in claim 5, line 9, is a relative term which renders the claim indefinite. The term "high iodine content" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably appraised of the scope of the invention.

6. Claim 16 recites the limitation "the group represented by R" in line 2 of the claim. There is insufficient antecedent basis for this limitation in the base claim. Applicant is suggested to change the dependency to claim 15 to overcome this rejection.

Information Disclosure Statement

7. The information disclosure statement ("IDS") filed October 09, 2001 fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609. Specifically, no copy of the PCT/US01/1638 was provided. Further, items C2-C8 fail to comply with 37 CFR 1.98(b), because they do not identify the inventor nor the filing date of the references. The IDS has been placed in the application file, but the above references have not been considered as to the merits. Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609 ¶ C(1).

8. Nevertheless, the following US Patents 6538026, 6037366, 6476069,6476070, which respectively correspond to Application SN 09/577,115, 09/151,621, 09/241368, and 09/497,075 (items C2-C3, C5-C6) have been considered and are hereby made of record.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

9. Claims 1-3, 9-10, 15-21, 23-26 are rejected under 35 U.S.C. 102(b) as being anticipated by Krall et al WO 00/44287 (WO '287).

10. Instant claims are directed to compositions comprising a matrix-forming component and a non-cyanoacrylate rheology-modifying agent. Dependent claim 10 is directed to such compositions wherein the non-cyanoacrylate rheology modifying agent is present in amounts of about 0% by weight of the matrix forming component (see claim 10). Accordingly, Examiner views the non-cyanoacrylate rheology modifying agent to be an optional component because it can exist in amounts of about 0% of the matrix-forming component. Thus, this recitation does not affirmatively limit the claims. Also, claim 16 is examined to the extent that it would depend on claim 15.

11. Krall discloses compositions comprising the two components of M1 and M2 (abstract; example 6, pages 50-53). M1 meets the limitation of the instant matrix-forming material because it contains 2-Hexyl Cyanoacrylate, which is an alkyl

cyanoacrylate monomer in amounts of about 49% wt in total formulation. (see page 18, lines 18-20, example 4, page 47). M1 further contains hyroquinone, p-methoxyphenol and phosphoric acid as the stabilizers (page 6, lines 24-33; page 7, lines 1-26; page 19, lines 20-25, page 62, claims 1-9). Krall uses and claims such amounts of hydroquinone and phosphoric acid that falls within the ranges of the instant claim 20 (see page 63, lines 11-20). Krall also discloses the use of n-butyl cyanacrylates in amounts of about 33% wt. (see examples 4-5, 7, pages 47-54).

The M2 component of Krall contains a radiopaque moiety, which can be pure gold powder, iodinated oil or other alike agents (page 17, lines 1-10; page 26, lines 18-26; page 27, lines 1-25). Krall specifically uses powdered gold, which meets the instant solid aggregate material limitation of claim 2 (page 50, line 15; example 6). The ethyl myristate and the Ethiodol of Krall also anticipate the plasticizer component of instant claim 26, because they are respectively an alkyl ester and an iodinated oil and fall within the plasticizers enumerated in the instant claim 25-26. (see page 64, lines 1-6; and page 65, lines 15-18). Therefore, Krall is an anticipatory reference as it discloses all the limitations of the instant claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

12. Claims 1-5, 7-11, 15-21, 23-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Krall et al WO 00/44287 (WO '287) in view of Evans US Patent 5,702,361.

13. The teachings of Krall WO '287 are described above. Krall fails to employ non-cyanoacrylate rheology modifying agents that are of polymeric material in amounts higher than 0% (as recited in claim 11) and/or have a specific molecular weight (as recited in claims 7-8).

14. Evans teaches suitable polymeric non-cyanoacrylate rheology modifying agent having similar molecular weight as those instantly claimed and are used in similar amounts as instantly claimed. Evans teaches the use of prepolymeric (monomeric) cyanoacrylate liquid in conjunction with other polymeric compositions. Evans establishes that biocompatible polymers such as cellulose diacetate (a cellulosic polymer) and biocompatible pre-polymers such as cyanoacrylates are functional equivalents in the art of polymeric embolizing compositions because they provide the same clinical endpoint in situ. (see col 5, line 24-col 7-line 1). Evans also teaches the use of non-cyanoacrylate polymers, such as ethylene vinyl alcohol copolymers (EVOH)

and hydrogels which are acrylic polymers (see col 5, lines 25-30, examples 1-2) in his compositions. Evans polymers are soluble with cyanoacylate liquid because Evans states that they can be directly combined with cyanoacrylate without the use any solvents, thus, Evans teaches the elements of claim 4-5, 11 (col 9, lines 53-55). Therefore, a non-cyanoacrylate polymer such as cellulose diacetate, EVOH , or acrylic polymer can be combined with a cyanoacrylate polymer for embolizing purposes.

Evans further teaches polymers having an average molecular weight of about 75,000-200,000. The desirable viscosity properties of Evan's polymers as embolic compositions are similar to those taught by Krall (see abstract and col 9, lines 50-60). Evans even states that the optimal viscosity of the composition can be achieved by merely adjusting the molecular weight or concentrations of the polymeric composition, which is a skill well within the level of an ordinary skill in the art (col 5, lines 23-59). Evans also uses his polymers in amount of about 4 to 5.2 % (see col 7, lines 10-20). Accordingly, polymers of Evans meet the limitations of instant claims 4-5, 7-8, 11.

Evans' compositions also contain a contrast agent such as tantalum or tantalum oxide, barium sulfates, metrizamide to provide visualization during their use (col 6, lines 26-36; col 12, lines 50-57). Therefore, the teachings of Evans are analogous to those of Krall.

15. It has been held to be *prima facie* obvious to combine two compositions each of which is taught by prior art to be useful for same purpose in order to form third composition that is to be used for very same purpose; idea of combining them flows

logically from their having been individually taught in prior art. In re Kerkhoven, 205 USPQ 1069 (CCPA 1980).

16. Thus, it would have been obvious to one of ordinary skill in the art at the time of invention to add a suitable polymeric embolic formulation, such as the cellulose diacetate or EVOH of Evans, to the formulation of Krall WO '287, because such a modification would have involved a mere addition of Evans polymeric compositions to those of Krall's and as reasoned in Kerkhoven, the idea of combining them flows logically by the prior art.

17. Claims 1-3, 9-10, 15-26 are rejected under 35 U.S.C. 103(a) as being unpatentable over Krall et al WO 00/44287 (WO '287) in view of Na et al US Patent 5,447,710.

18. The teachings of Krall. Krall fails to address the limitations of claim 14 where the use of a non-cyanoacrylate rheology-modifying agent that comprises inorganic particles with surface-modifying molecules adsorbed to or bonded to the surface of such particles.

19. Na et al is merely used to show that nonionic surfactant may be administered as a surface modifier to be absorbed on the surface of diagnostic particles such as iodinated radiopaque agents. Na states that such modifications of radiopaque particles improve the particle size and quality of the contrast technique (see abstract; col 3, lines 35-40; col 5, lines 45-60; col 8, lines 1-30). Na teaches preparing his compositions in combination with other therapeutic ingredients (col 4, lines 44-56; col 7, lines 44-60). Na does not explicitly use his compositions in an embolic formulation.

20. However, as Na's iodinated contrast agents are similar to those taught in Krall WO '287, it would have also been obvious to one of ordinary skill in the art at the time of invention to substitute the radiopaque agents employed in Krall WO '287, with the surface modified iodinated contrast agents taught by Na, because Na suggests that the ordinary skill in the art would have had a reasonable expectation of success in improving the contrast properties of particulate containing compositions when such particles contain a surface modifier.

21. Claims 1-3, 9-10, 15-21, 23-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over Krall et al WO 00/44287 (WO '287) in view of Krall US Patent 6,037,366 (US '366).

22. The teachings of Krall WO '287 are described above. Krall does not teach plasticizers within the ranges of 10% to about 75% of the matrix-forming component.

23. Krall US '366 is used to show that it is well within the level of a skilled artisan to employ simple manufacturing procedure and use sufficient amount of a fatty acid ester plasticizer, such as ethyl myristate, in amount of about 16.4% wt of the total formulation (50 % wt/wt x (0.5 g / 1.52 g) = 16.4% of the total formulation) (see col 2, lines 39-65; col 3, lines 1-14, and 45-52). Thus, Krall provides for the limitations of the instant claims 26-28.

24. Thus, absence of showing criticality, it would have been obvious to one of ordinary skill in the art at the time of invention to optimize the concentrations of plasticizers in the embolic composition of Krall WO '267 by routine experimentation, because as taught in Krall US '366 the ordinary skill in the art would have had a

reasonable expectation of success in optimizing the flow characteristics of embolic formulations by modifying the amount of a plasticizer, such as ethyl myristate.

Conclusion

25. No claims are allowed. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shahnam Sharareh whose telephone number is 703-306-5400. The examiner can normally be reached on 8:30 am - 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, PhD can be reached on 703-308-1877. The fax phone number for the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1123.

Shahnam Sharareh, PharmD
Patent Examiner, Art Unit 1617

8/10/03